

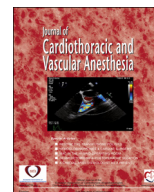
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Original Article

## Fluid Responsiveness After Cardiac Surgery (FRACAS): A Prospective Observational Study Using Peripheral Near-Infrared Spectroscopy

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**Objectives:** To describe tissue oxygen saturation (StO<sub>2</sub>) in response to a vascular occlusion test using thenar eminence and forearm near-infrared spectroscopy (NIRS) and the association with volume responsiveness after cardiac surgery.

**Design:** Single-center, prospective, observational cohort study.

**Setting:** Cardiothoracic intensive care unit.

**Participants:** Seventy-six post-cardiac surgical adults.

**Interventions:** Immediately before and 10 minutes after a 250-to-500 mL fluid bolus, StO<sub>2</sub> was measured in response to a vascular occlusion test to calculate tissue deoxygenation (R<sub>des</sub>) and reoxygenation (R<sub>res</sub>) rates. Concurrently, systemic hemodynamic, metabolic, and blood gas variables were collected.

**Measurements and Main Results:** A total of 203 boluses were captured using thenar NIRS and 141 boluses using forearm NIRS. Approximately 25% of boluses increased cardiac output by  $\geq 15\%$  (volume responders). Thenar and forearm R<sub>des</sub> decreased in responders, but increased (thenar) or remained unchanged (forearm) in nonresponders. A logistic regression model of the association among StO<sub>2</sub>, R<sub>des</sub> and R<sub>res</sub>, and volume responsiveness was significant for thenar measurements ( $p = 0.001$ ) with an area under the receiver operating characteristic of 0.69 (95% confidence interval: 0.62-0.75). It also was significant ( $p = 0.02$ ) for forearm measurements, with an area under the receiver operating characteristic of 0.71 (0.62-0.79). R<sub>des</sub> was an independent variable in both instances (odds ratio 0.31 [0.14-0.69], thenar; odds ratio 0.60 [0.45-0.80], forearm). Thenar and forearm NIRS variables were correlated poorly with cardiac output, stroke volume, systemic oxygen delivery and consumption index, mixed venous, and central venous oxygen saturation (Spearman's coefficients,  $r = 0.17$ - $0.46$ ,  $p < 0.002$ ).

**Conclusion:** In post-cardiac surgical patients, thenar and forearm NIRS variables were associated with volume responsiveness although not achieving precision necessary for clinical management.

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**Key Words:** spectroscopy, near-infrared; fluid responsiveness; microcirculation; cardiac surgery; postsurgical patients

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INTRAVASCULAR VOLUME EXPANSION remains the cornerstone of hemodynamic optimization for post-cardiac surgery patients in the intensive care unit (ICU), despite only half of fluid boluses significantly improving cardiac output.<sup>1,2</sup> While hypovolemic hypoperfusion leads to organ dysfunction,

overzealous fluid resuscitation also is associated with increased morbidity and mortality.<sup>3–5</sup> Current evidence suggests that a lack of hemodynamic coherence between macrocirculatory and microcirculatory variables<sup>6,7</sup> means that occult tissue hypoperfusion might persist despite normalization of macrocirculatory variables. Equally, apparently ineffective fluid loading (ie, without significant increase in cardiac output) may still improve microcirculatory oxygenation.<sup>8</sup> For these reasons, the addition of minimally invasive methods to assess microvascular integrity and tissue oxygenation during volume expansion for hemodynamic optimization would be beneficial.

Peripheral near-infrared spectroscopy (NIRS) provides non-invasive, continuous, and real-time assessments of tissue hemoglobin oxygen saturation (StO<sub>2</sub>).<sup>9</sup> Performing a vascular occlusion test (VOT) allows for further assessment of microcirculatory integrity during and after a brief ischemic challenge.<sup>9</sup> In particular, the hemoglobin deoxygenation slope (R<sub>des</sub>), which provides an approximation of local oxygen extraction, and reoxygenation slope (R<sub>res</sub>), which reflects post-ischemic capillary recruitment and vasodilation, can be calculated from the change in StO<sub>2</sub> during the VOT<sup>9</sup> and have been shown to offer more clinical utility than StO<sub>2</sub> alone.<sup>8,10,11</sup> Furthermore, the desaturation area under the curve (D<sub>AUC</sub>) and hyperemic area under the curve (H<sub>AUC</sub>), which reflect local oxygen extraction and post-ischemic hyperemia, respectively, may serve as additional markers of microvascular integrity.<sup>9</sup>

In post-cardiac surgery patients responding to volume expansion, defined by an increase in cardiac index by  $\geq 15\%$ , calf StO<sub>2</sub> increased whereas it remained unchanged in nonresponders.<sup>12</sup> However, R<sub>des</sub>, D<sub>AUC</sub>, R<sub>res</sub>, and H<sub>AUC</sub> were not assessed. Intraoperatively, fluid administration improved thenar R<sub>res</sub>, most notably in volume-responsive patients, but no significant changes in thenar R<sub>des</sub> or H<sub>AUC</sub> were reported.<sup>8</sup>

The authors conducted this study in postoperative cardiac surgical patients to (1) describe changes in thenar and forearm NIRS variables following volume expansion, and (2) determine if any such changes were associated with fluid responsiveness. The authors hypothesized that volume-responsive patients would improve microcirculatory oxygen extraction (more negative R<sub>des</sub>, more positive D<sub>AUC</sub>) and reactivity (more positive R<sub>res</sub> and H<sub>AUC</sub>), and that some fluid nonresponders may still improve microcirculatory perfusion.

## Methods

### Study Design

This prospective, observational cohort study of Fluid Responsiveness After CARDiac Surgery (FRACAS) was performed in the cardiothoracic ICU of Liverpool Hospital, Sydney, Australia. The Human Research Ethics Committee of South Western Sydney Local Health District approved the study as a Low-Negligible Risk project (HREC/LNR/14/LPOOL/295). Written patient consent was waived because data were obtained during routine care as per institutional standards. The study is registered at ClinicalTrials.gov

(NCT02841943) and reported following the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement for observational studies.<sup>13</sup>

### Study Population

Post-cardiac surgical patients admitted to the ICU between March 2016 and August 2016 were screened consecutively for enrollment (Fig 1). Patients  $\geq 18$  years of age, undergoing cardiac surgery (coronary artery bypass graft, valve repair/replacement, combined cardiac surgery), and arriving to the ICU with an arterial and pulmonary artery catheter, were eligible for inclusion. Patients admitted to the ICU following emergency surgery, with ongoing extracorporeal circulatory support, with intracardiac shunts, readmitted within the same index hospital admission, or unable to be fitted with a NIRS optode for VOT were excluded. Only 1 patient at a time could be studied due to equipment logistics. Patients were treated according to institutional post-cardiac surgical guidelines as reported elsewhere,<sup>14</sup> including initial volume-controlled ventilation (positive end-expiratory pressure of 5 cmH<sub>2</sub>O, respiratory rate 12–16/min, tidal volume 6–8 mL/kg) and sedation with propofol and fentanyl or morphine. Ventilation was weaned and patients were evaluated for extubation within 6 hours of admission. A mean arterial pressure (MAP) greater than 70 mmHg and a cardiac index greater than 2.5 L/min/m<sup>2</sup> were targeted unless postoperative orders specified otherwise.

### Study Protocol

Upon admission to the ICU, a NIRS optode with an approximate tissue light penetration of 25 mm (CAS Medical Systems Inc, Branford, CT) was attached to the thenar eminence and/or ventral forearm overlying the flexor digitorum profundus. Care was taken to ensure optodes were not obstructed by hair and were further wrapped to minimize ambient light contamination and movement. Thenar and forearm thickness (mm) was the average of 3 measurements at the site of optode fixation using a standard calliper.

Administration of a fluid bolus was left entirely to the discretion of the treating ICU team who were not involved in the FRACAS study and blinded to all NIRS measurements. In case a fluid bolus was prescribed, the NIRS measurements were performed immediately prior to and 10 minutes after its administration. A 3-minute baseline StO<sub>2</sub> was obtained and a VOT then was performed, which involved rapidly inflating (< 3 seconds) a sphygmomanometer cuff until 50 mmHg above the systolic blood pressure (obtained from the arterial line on the alternate arm). The cuff was released rapidly (< 2 seconds) after 3 minutes of occlusion. The NIRS measurements were made using a ForeSight MC-2030 Universal Oximeter (CAS Medical Systems Inc, Branford, CT) connected to a laptop computer running the ICM+ data capture software (Cambridge Enterprise Ltd, University of Cambridge, Cambridge, UK).

A fluid bolus was defined as 250 mL (over 10 minutes) or 500 mL (over 20 minutes) of fluid (crystalloid or colloid)

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